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	NEW	IS	1			Web Page for STN Seminar Schedule - N. America
NEWS			AUG	10	Time limit for inactive STN sessions doubles to 40	
					minutes	
NEWS		3	AUG	18	COMPENDEX indexing changed for the Corporate Source	
						(CS) field
	NEW	IS	4	AUG	24	ENCOMPLIT/ENCOMPLIT2 reloaded and enhanced
	NEWS 5		AUG	24	CA/CAplus enhanced with legal status information for	
						U.S. patents
	NEW	IS	6	SEP	09	50 Millionth Unique Chemical Substance Recorded in
						CAS REGISTRY
	NEW	IS	7	SEP	11	WPIDS, WPINDEX, and WPIX now include Japanese FTERM
						thesaurus
	NEW	15	8	OCT	21	Derwent World Patents Index Coverage of Indian and
	NEW		9	OCT	21	Taiwanese Content Expanded Derwent World Patents Index enhanced with human
	NEW	15	9	OCI	21	translated claims for Chinese Applications and
						Utility Models
	NEW	10	1.0	NOV	23	Addition of SCAN format to selected STN databases
			11	NOV		Annual Reload of IFI Databases
				DEC		FRFULL Content and Search Enhancements
			13	DEC		DGENE, USGENE, and PCTGEN: new percent identity
				DEC	0.1	feature for sorting BLAST answer sets
	NEW	IS	14	DEC	0.2	Derwent World Patent Index: Japanese FI-TERM
		_				thesaurus added
	NEW	IS	15	DEC	02	PCTGEN enhanced with patent family and legal status
						display data from INPADOCDB
	NEW	IS	16	DEC	02	USGENE: Enhanced coverage of bibliographic and
						sequence information
	NEW	IS	17	DEC	21	New Indicator Identifies Multiple Basic Patent
						Records Containing Equivalent Chemical Indexing
						in CA/CAplus
	NEW	IS	18	JAN	12	Match STN Content and Features to Your Information
						Needs, Quickly and Conveniently
			19	JAN		Annual Reload of MEDLINE database
	MEN	15	20	FEB	Tρ	STN Express Maintenance Release, Version 8.4.2, Is Now Available for Download
	NIEW	7.0	21	FEB	16	Derwent World Patents Index (DWPI) Revises Indexing
	MEM	10	21	FED	10	of Author Abstracts
	NEG	ıs	22	FEB	16	New FASTA Display Formats Added to USGENE and PCTGEN
			23	FEB		INPADOCDB and INPAFAMDB Enriched with New Content
				- 55	-0	and Features
	NEW	IS	24	FEB	16	INSPEC Adding Its Own IPC codes and Author's E-mail
						Addresses

NEWS EXPRESS FEBRUARY 15 10 CURRENT WINDOWS VERSION IS V8.4.2, AND CURRENT DISCOVER FILE IS DATED 15 JANUARY 2010.

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FULL ESTIMATED COST

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TSCA INFORMATION NOW CURRENT THROUGH January 8, 2010.

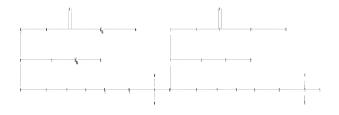
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= 3

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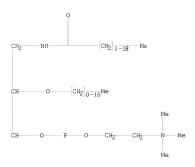
```
chain nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 21 22
chain bonds :
1-2 1-5 2-3 3-4 3-17 5-6 5-7 6-21 7-8 8-9 9-10 10-11 11-12 12-13 13-14 13-15 13-16 17-18 21-22
exact/norm bonds :
2-3 3-4 5-6 7-8 8-9 9-10
exact bonds :
1-2 1-5 3-17 5-7 6-21 10-11 11-12 12-13 13-14 13-15 13-16 17-18 21-22
```

Match level : 1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 21:CLASS 22:CLASS

L1 STRUCTURE UPLOADED

=> d 11 L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

```
=> s l1 sss
SAMPLE SEARCH INITIATED 12:42:33 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -
                                        8 TO ITERATE
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100.0% PROCESSED 8 ITERATIONS SEARCH TIME: 00.00.01

4 ANSWERS

```
FULL FILE PROJECTIONS:
                        ONLINE **COMPLETE**
                         BATCH
                                 **COMPLETE**
PROJECTED ITERATIONS:
                                  8 TO
                                            329
PROJECTED ANSWERS:
                                  4 TO
                                            200
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4 SEA SSS SAM L1 L2

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ANSWER 1 OF 4 REGISTRY COPYRIGHT 2010 ACS on STN
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RN 210418-12-5 REGISTRY

Entered STN: 26 Aug 1998 ED

CN 3,5-Dioxa-9-aza-4-phosphaheptacosan-1-aminium, 4-hydroxy-7-methoxy-N,N,N-trimethyl-10-oxo-, chloride, 4-oxide (9CI) (CA INDEX NAME) MF

C27 H58 N2 O6 P . C1

SR CAS Client Services

CRN (742681-49-8)

=> d 12 1-4

€ c1=

ANSWER 2 OF 4 REGISTRY COPYRIGHT 2010 ACS on STN

RN 207298-97-3 REGISTRY

ED Entered STN: 17 Jun 1998

CN

3,5-Dioxa-9-aza-4-phosphanonadecan-1-aminium, 4-hydroxy-N, N, N-trimethyl-7-(octyloxy)-10-oxo-, inner salt, 4-oxide (9CI) (CA INDEX NAME)

MF C26 H55 N2 O6 P CA SR

LC STN Files: CA, CAPLUS, TOXCENTER

$$\begin{array}{c} \text{Me} \\ -\text{O} & (\text{CH}_2) \text{ 7-O} \\ \text{O} & \text{O} \\ \text{Me} \text{ 3}^+\text{N} - \text{CH}_2 - \text{CH}_2 - \text{O} - \text{P-O} - \text{CH}_2 - \text{CH-CH}_2 - \text{NH-C} - (\text{CH}_2) \text{ 8-Me} \\ \text{O} \end{array}$$

2 REFERENCES IN FILE CA (1907 TO DATE) 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2010 ACS on STN

RN 207298-94-0 REGISTRY

ED Entered STN: 17 Jun 1998

CN 3,5-Dioxa-9-aza-4-phosphaheneicosan-1-aminium, 7-(hexyloxy)-4-hydroxy-N, N, N-trimethyl-10-oxo-, inner salt, 4-oxide (9CI) (CA INDEX NAME)

C26 H55 N2 O6 P

MF SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

2 REFERENCES IN FILE CA (1907 TO DATE) 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

1.2 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2010 ACS on STN

RN 207298-93-9 REGISTRY

ED Entered STN: 17 Jun 1998 CN 3,5-Dioxa-9-aza-4-phosphaheneicosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-7-(octyloxy)-10-oxo-, inner salt, 4-oxide (9CI) (CA INDEX NAME)

MF C28 H59 N2 O6 P

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

 $\begin{array}{c} & \text{Me} \\ -\text{O} & (\text{CH}_2) \ 7-\text{O} \\ \text{O} & \text{O} \\ \text{Me} \ 3^+\text{N}-\text{CH}_2-\text{CH}_2-\text{O} \\ \text{P}-\text{O}-\text{CH}_2-\text{CH}-\text{CH}_2-\text{NH}-\text{C}-(\text{CH}_2)} \ 10^-\text{Me} \\ \end{array}$

4 REFERENCES IN FILE CA (1907 TO DATE) 4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d his

(FILE 'HOME' ENTERED AT 12:41:35 ON 16 MAR 2010)

FILE 'REGISTRY' ENTERED AT 12:42:15 ON 16 MAR 2010 L1 STRUCTURE UPLOADED

L2 4 S L1 SSS

=> s 11 full

THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 191.05 U.S. DOLLARS DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y FULL SEARCH INITIATED 12:42:59 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 96 TO ITERATE

100.0% PROCESSED 96 ITERATIONS SEARCH TIME: 00.00.02 47 ANSWERS

TOTAL

SESSION

SINCE FILE

ENTRY

L3 47 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS

FULL ESTIMATED COST 199.94 200.16

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FILE COVERS 1907 - 16 Mar 2010 VOL 152 ISS 12

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FILE LAST UPDATED: 15 Mar 2010 (20100315/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2009
CAplus now includes complete International Patent Classification (IPC)
reclassification data for the first quarter of 2010.
CAS Information Use Policies apply and are available at:
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This file contains CAS Registry Numbers for easy and accurate
substance identification.
=> s 13
L4
           23 1.3
=> dup rem 14
PROCESSING COMPLETED FOR L4
            23 DUP REM L4 (0 DUPLICATES REMOVED)
=> s 15 and (virus or viral)
L6
           23 S L5
        434512 VIRUS
         91338 VIRUSES
        451209 VIRUS
                (VIRUS OR VIRUSES)
        218316 VIRAL
            29 VIRALS
        218333 VIRAL
                (VIRAL OR VIRALS)
            10 L6 AND (VIRUS OR VIRAL)
=> d 17 1-10 ibib abs hitstr
L7 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:
                        2006:198407 CAPLUS
DOCUMENT NUMBER:
                         144:403777
TITLE:
                         Using small molecules to overcome drug resistance
                        induced by a viral oncogene
                        Smukste, Inese; Bhalala, Oneil; Persico, Marco;
AUTHOR(S):
                        Stockwell, Brent R.
CORPORATE SOURCE:
                         Department of Biological Sciences and Department of
                         Chemistry, Fairchild Center, Columbia University, New
                         York, NY, 10027, USA
                         Cancer Cell (2006), 9(2), 133-146
SOURCE:
                         CODEN: CCAECI; ISSN: 1535-6108
                        Cell Press
PUBLISHER:
DOCUMENT TYPE:
                        Journal
LANGUAGE:
                         English
    We used small mol. screening to discover compds. and mechanisms for
     overcoming E6 oncogene-mediated drug resistance. Using high-throughput
     screening in isogenic cell lines, we identified compds. that potentiate
     doxorubicin's lethality in E6-expressing colon cancer cells. Such compds.
     included quaternary ammonium salts, protein synthesis inhibitors,
     11-deoxyprostaglandins, and two addnl. classes of compds.-analogs of
     1,3-bis(4-morpholinylmethyl)-2-imidazolidinethione (a thiourea) and
     acylated secondary amines that we named indoxins. Indoxins upregulated
```

topoisomerase II α , the target of doxorubicin, thereby increasing doxorubicin lethality. We developed a photolabeling strategy to identify targets of indoxin and discovered a nuclear actin-related protein complex

as a candidate indoxin target.

IT 88876-07-7

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(small mols, which overcome drug resistance induced by a viral oncogene)

88876-07-7 CAPLUS PM

3,5-Dioxa-9-aza-4-phosphaheptacosan-1-aminium, CN

4-hydroxy-7-methoxy-N, N, N-trimethyl-10-oxo-, inner salt, 4-oxide (CA INDEX NAME)

OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)

58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2005:904330 CAPLUS

DOCUMENT NUMBER: 143:222464

TITLE: Phospholipids for the treatment of infection by

togaviruses, herpes viruses and coronaviruses

INVENTOR(S):

Fleming, Ronald A.; Hes, Jan V.; Huang, Yunsheng; Read, Russ H.; Morris-Natschke, Susan L.; Ishaq,

Khalid S.; Kucera, Louis S.; Furman, Phillip A.

PATENT ASSIGNEE(S): Kucera Pharmaceutical Company, USA

SOURCE: U.S. Pat. Appl. Publ., 36 pp. CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

virus was 0.48 µg/mL.

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
US 20050187192	A1	20050825	US 2004-783927	20040220		
PRIORITY APPLN. INFO.:			US 2004-783927	20040220		
OTHER SOURCE(S):	MARPAT	143:222464				

AB Provided are compds., methods and pharmaceutical compns. for treating a host, especially a human, infected with a togavirus, herpes virus and/or coronavirus, and in particular SARS-CoV, cytomegalovirus or varicella-zoster virus. The method in one embodiment comprises administering to that host an effective amount of an anti-togavirus, anti-herpes virus and/or anti-coronavirus phospholipid or a pharmaceutically acceptable salt or prodrug thereof. The phospholipid compound is, e.g., a 3-alkylamido-2-alkoxypropylphosphocholine compound or salt thereof. The compound may be administered alone or in combination and/or alternation with one or more other antiviral agents. The EC50 of an alkylamido-2-alkoxypropylphosphocholine against varicella zoster

TT 252371-27-0 443882-90-4 443882-91-5

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(phospholipids for treatment of infection by togaviruses, herpes viruses and coronaviruses)

RN 252371-27-0 CAPLUS

CN 3,5-Dioxa-9-aza-4-phosphanonadecan-1-aminium, 7-(decyloxy)-4-hydroxy-N, N, N-trimethyl-10-oxo-, inner salt, 4-oxide (9CI) (CA INDEX NAME)

$$\begin{array}{c} Me \\ -0 & (CH_2)_9 - 0 \\ 0 & | \\ Me_3 + N - CH_2 - CH_2 - O - P - O - CH_2 - CH - CH_2 - NH - C - (CH_2)_8 - Me \\ 0 & | \\ \end{array}$$

- 443882-90-4 CAPLUS RN
- CM 3,5-Dioxa-9-aza-4-phosphanonadecan-1-aminium, 7-ethoxy-4-hydroxy-N, N, N-trimethyl-10-oxo-, inner salt, 4-oxide (9CI) (CA INDEX NAME)

- RN 443882-91-5 CAPLUS
- 3.5-Dioxa-9-aza-4-phosphaheneicosan-1-aminium, CN 7-ethoxy-4-hydroxy-N, N, N-trimethyl-10-oxo-, inner salt, 4-oxide (9CI) (CA INDEX NAME)

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L7 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2005:902611 CAPLUS DOCUMENT NUMBER:

143:241938

TITLE: Methods and compositions for the treatment of

respiratory syncytial virus

INVENTOR(S): Kucera, Louis S.; Morris-Natschke, Susan L.; Ishaq, Khalid S.; Fleming, Ronald A.; Hess, Jan V.; Huang,

Yunsheng; Read, Russ H.; Furman, Phillip A.

PATENT ASSIGNEE(S):

SOURCE: U.S. Pat. Appl. Publ., 29 pp. CODEN: USXXCO

DOCUMENT TYPE: Pat.ent.

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

KIND DATE APPLICATION NO. DATE PATENT NO.

US	2005	0187	191		A1		2005	0825	1	US 2	004-	7818	94		2	0040	220	
WO	2005099719			A2		2005	1027	WO 2005-US3972					20050209					
WO	2005099719			A3	A3 20070322													
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,	
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,	
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NI,	
		NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SM,	
		SY,	TJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	zw
	RW:	BW,	GH,	GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	
		AZ,	BY,	KG,	ΚZ,	MD,	RU,	TJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	
		EE,	ES,	FI,	FR,	GB,	GR,	HU,	IE,	IS,	IT,	LT,	LU,	MC,	NL,	PL,	PT,	
		RO,	SE,	SI,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	
		MR,	NE,	SN,	TD,	TG												

PRIORITY APPLN. INFO.: OTHER SOURCE(S): US 2004-781894 A 20040220 MARPAT 143:241938

AB The invention includes compds. useful for inhibiting RSV replication and treating a host infected with RSV. The invention also includes methods of treating a host infected with RSV by administering to the host an anti-RSV effective amount of a compound of the invention.

IT 443882-90-4, KPC 11 443882-91-5, KPC 15 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological

activity); THU (Therapeutic use); BIOL (Biological Study); USES (Uses) (compns. for treatment of respiratory syncytial virus)

RN 443882-90-4 CAPLUS

CN 3,5-Dioxa-9-aza-4-phosphanonadecan-1-aminium, 7-ethoxy-4-hydroxy-N,N,N-trimethyl-10-oxo-, inner salt, 4-oxide (9CI) (CA INDEX NAME)

RN 443882-91-5 CAPLUS

CN 3,5-Dioxa-9-aza-4-phosphaheneicosan-1-aminium, 7-ethoxy-4-hydroxy-N,N,N-trimethyl-10-oxo-, inner salt, 4-oxide (9CI) (CA INDEX NAME)

IT 207298-91-7 207298-93-9 252371-27-0

443882-96-0

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(compns. for treatment of respiratory syncytial virus)

RN 207298-91-7 CAPLUS

CN 3,5-Dioxa-9-aza-4-phosphaheneicosan-1-aminium, 7-(dodecyloxy)-4-hydroxy-N,N,N-trimethyl-10-oxo-, inner salt, 4-oxide

(9CI) (CA INDEX NAME)

- RN 207298-93-9 CAPLUS
- CN 3,5-Dioxa-9-aza-4-phosphaheneicosan-1-aminium, 4-hydroxy-N, N, N-trimethyl-7-(octyloxy)-10-oxo-, inner salt, 4-oxide (9CI) (CA INDEX NAME)

- 252371-27-0 CAPLUS RN
- CN 3,5-Dioxa-9-aza-4-phosphanonadecan-1-aminium, 7-(decyloxy)-4-hydroxy-N,N,N-trimethyl-10-oxo-, inner salt, 4-oxide (9CI) (CA INDEX NAME)

- RN 443882-96-0 CAPLUS
- CN 3,5-Dioxa-9-aza-4-phosphaheneicosan-1-aminium, 7-butoxy-4-hydroxy-N, N, N-trimethyl-10-oxo-, inner salt, 4-oxide (9CI) (CA INDEX NAME)

L7 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER:

1998:435743 CAPLUS

DOCUMENT NUMBER:

129:90448

TITLE:

ORIGINAL REFERENCE NO.: 129:18491a,18494a

Method of treating hepatitis virus infections

INVENTOR(S):

Kucera, Louis S.; Morris-Natschke, Susan L.

PATENT ASSIGNEE(S):

Wake Forest University, USA; University of North

Carolina

SOURCE: U.S., 17 pp., Cont.-in-part of U.S. Ser. No. 74,943, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 5770584	A	19980623	US 1995-465947		19950606
US 6030960	A	20000229	US 1998-102308		19980622
PRIORITY APPLN. INFO.:			US 1993-74943 E	32	19930610
			US 1995-465947 I	43	19950606

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): MARPAT 129:90448

AB A method of treating hepatitis virus infection is disclosed. The method involves administering to a human subject in need of such treatment an effective hepatitis virus-combating amount of an alkyl lipid derivative.

IT 112989-01-2P 112989-02-3P 209532-02-5P

209532-03-6P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(alkyl lipids for treating hepatitis virus infections)

RN 112989-01-2 CAPLUS

ON 3,5-Dioxa-9-aza-4-phosphapentacosan-1-aminium,

7-ethoxy-4-hydroxy-N,N,N-trimethyl-10-oxo-, inner salt, 4-oxide (CA INDEX NAME)

RN 112989-02-3 CAPLUS

CN 3,5-Dioxa-9-aza-4-phosphaheptacosan-1-aminium, 7-ethoxy-4-hydroxy-N,N,N-trimethy1-10-oxo-, inner salt, 4-oxide (CA INDEX NAME)

RN 209532-02-5 CAPLUS

CN 3,5-Dioxa-9-aza-4-phosphaheptacosan-1-aminium, 7-ethoxy-4-hydroxy-N,N,N-trimethyl-10-oxo-, inner salt, 4-oxide, (+)-(9CI) (CA INDEX NAME)

Rotation (+).

209532-03-6 CAPLUS

CN 3.5-Dioxa-9-aza-4-phosphapentacosan-1-aminium, 7-ethoxy-4-hydroxy-N, N, N-trimethyl-10-oxo-, inner salt, 4-oxide, (+)-(9CI) (CA INDEX NAME)

Rotation (+).

OS.CITING REF COUNT: THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 5 OF 10 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1998:205430 CAPLUS

DOCUMENT NUMBER: 128:316940

ORIGINAL REFERENCE NO.: 128:62637a,62640a TITLE:

In vitro evaluation and characterization of newly designed alkylamidophospholipid analogs as anti-human

immunodeficiency virus type 1 agents

AUTHOR(S): Kucera, L. S.; Iyer, N.; Morris-Natschke, S. L.; Chen,

S. Y.; Gumus, F.; Ishaq, K.; Herrmann, D. B. J. CORPORATE SOURCE: Wake Forest University School Medicine, Winston-Salem,

NC, USA

SOURCE: Antiviral Chemistry & Chemotherapy (1998), 9(2),

157-165

CODEN: ACCHEH: ISSN: 0956-3202

PUBLISHER: International Medical Press DOCUMENT TYPE: Journal

LANGUAGE: English

Our labs. first reported two novel classes of complex synthetic lipids, including alkylamidophosphocholines (PC lipid; CP-51) and

alkylamidophosphate ester-linked lipid-AZT conjugates (lipid-AZT conjugates; CP-92), with selective and potent activity against human

immunodeficiency virus type 1 (HIV-1). To extend these observations, we synthesized addnl. PC lipids and lipid-AZT conjugates

(INK and INK-AZT conjugate) to evaluate their structure-activity relationships by testing for selectivity against infectious wild-type (wt)

and drug-resistant HIV-1 replication, virus fusogenic activity

and toxicity replication, virus fusogenic activity and toxicity for mouse bone marrow cells. PC lipid compds. with medium chain lengths at positions 1 and 2 gave an improved selective index (SI). INK-3, with 12 and 8 carbons and INK-15, with 10 and 12 carbons were among the most selective when evaluated in CEM-SS cells. INK-14, a lipid-AZT conjugate where AZT replaced the choline in PC lipid INK-3, gave the highest SI of >1250 against both infectious wt HIV-1 replication in CEM-SS cells and a clin. isolate in peripheral blood leukocytes. Notably, the PC lipid compds. INK-3 and INK-15, but not the lipid-AZT conjugate INK-14, were potent inhibitors of matched pairs of AZT-sensitive and AZT-resistant HIV-1 clin. isolates. INK-3 also inhibited replication of HIV-2 and TIBO-resistant HIV-1, and inhibited HIV-1-mediated fusogenic activity by 78, 41 and 9% in a dose-dependent manner. The TCS0 for mouse bone marrow cells was >100 $\mu g/mL$ for CP-51 and 0.142-0.259 $\mu g/mL$ for AZT. These data suggest that optimum PC lipid compds. are significantly less toxic than AZT and have high potential as novel therapeutic agents for AIDS.

IT 207298-91-7P 207298-92-8P 207298-93-9P 207298-94-0P 207298-95-1P 207298-97-3P 207298-95-P

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(anti-HIV-1 activity and preparation of alkylamidophospholipid analogs) RN 207298-91-7 CAPLUS

CN 3,5-Dioxa-9-aza-4-phosphaheneicosan-1-aminium, 7-(dodecyloxy)-4-hydroxy-h,N,N-trimethyl-10-oxo-, inner salt, 4-oxide (9CI) (CA INDEX NAME)

RN 207298-92-8 CAPLUS

CN 3,5-Dioxa-9-aza-4-phosphaheneicosan-1-aminium, 7-(decyloxy)-4-hydroxy-N,N,N-trimethyl-10-oxo-, inner salt, 4-oxide (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{-0} & (\text{CH}_2) \, 9 - 0 \\ \text{O} & (\text{CH}_2) \, 10 - 0 \\ \text{Me} \, 3^{+}\text{N} - \text{CH}_2 - \text{CH}_2 - \text{O} - P - O - \text{CH}_2 - \text{CH} - \text{CH}_2 - \text{NH} - C - (\text{CH}_2) \, 10 - \text{Me} \\ \end{array}$$

RN 207298-93-9 CAPLUS

CN

3,5-Dioxa-9-aza-4-phosphaheneicosan-1-aminium,
4-hydroxy-N,N,N-trimethyl-7-(octyloxy)-10-oxo-, inner salt, 4-oxide (9CI)
(CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{-0} & (\text{CH}_2) \, 7\text{-0} \\ \text{0} & \text{0} \\ \text{Me} \, 3\text{+N-CH}_2\text{-CH}_2\text{-O-P-O-CH}_2\text{-CH-CH}_2\text{-NH-C-} \, (\text{CH}_2) \, 10\text{-Me} \\ \text{0} \end{array}$$

- RN 207298-94-0 CAPLUS
- CN 3,5-Dioxa-9-aza-4-phosphaheneicosan-1-aminium, 7-(hexyloxy)-4-hydroxy-N,N,N-trimethyl-10-oxo-, inner salt, 4-oxide (9CI) (CA INDEX NAME)

- RN 207298-95-1 CAPLUS
- CN 3,5-Dioxa-9-aza-4-phosphaheptacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-7-(octyloxy)-10-oxo-, inner salt, 4-oxide (9CI) (CA INDEX NAME)

- RN 207298-97-3 CAPLUS
- CN 3,5-Dioxa-9-aza-4-phosphanonadecan-1-aminium, 4-hydroxy-N,N,N-trimethyl-7-(octyloxy)-10-oxo-, inner salt, 4-oxide (9CI) (CA INDEX NAME)

- RN 207298-99-5 CAPLUS
- CN 3,5-Dioxa-9-aza-4-phosphanonadecan-1-aminium, 7-(dodecyloxy)-4-hydroxy-N,N,N-trimethyl-10-oxo-, inner salt, 4-oxide (9C1) (CA INDEX NAME)

II 112989-02-3, CP 51
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or

effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(anti-HIV-1 activity and preparation of alkylamidophospholipid analogs)

RN 112989-02-3 CAPLUS CN 3.5-Dioxa-9-aza-4-pt

3,5-Dioxa-9-aza-4-phosphaheptacosan-1-aminium,

7-ethoxy-4-hydroxy-N,N,N-trimethyl-10-oxo-, inner salt, 4-oxide (CA INDEX NAME)

OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS

RECORD (13 CITINGS)

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1995:701769 CAPLUS DOCUMENT NUMBER: 123:112632

DOCUMENT NUMBER: 123:112632 ORIGINAL REFERENCE NO.: 123:20141a,20144a

TITLE: Phospholipids for combating hepatitis B virus

infection

INVENTOR(S): Kucera, Louis S.; Morris-Natschke, Susan L.

PATENT ASSIGNEE(S): Wake Forest University, USA; University of North Carolina

SOURCE: PCT Int. Appl., 38 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PA:	PATENT NO.						KIND DATE			APPL	ICAT		DATE				
	VO 9428908 VO 9428908								WO 1	994-		19940525					
	W:	HU,	JP,	KG,	KP,	KR,	BY, KZ,	LK,	LU,	LV,	MD,	MG,	MN,	MW,	NL,		
	RW:	AT,	BE,	CH,	DE,	DK,	SE, ES, CM,	FR,	GB,	GR,	IE,	IT,	LU,	MC,	NL,	PT,	SE,
	2164 2164	717	·		A1		1994 2009	1222								9940	525
AU	9470	448			A		1995	0103									
	7025	56			В1			1023					-				
AT PRIORIT	2264 APP				T	·	2002	1115		US 1	993-	7494	3		A 1	9930	610
OTHER SOURCE(S):						PAT	123:	1126		WO 1	994-	US58	55	1	W 1	3940.	525

A method of treating infection with hepatitis B virus is AB disclosed. The method comprises administration of alkyl ether phospholipids and derivs. of formula DCH2XCH2YR1 [Y = S, O, NH, NMe, NHCO, NMeCO; R1 = (un)branched (un)saturated C10-20 alk(en/yn)y1; X = bond, CH2 (un) substituted by OH, alkyl, alkoxy, or alkylthio; D = (PO4)-E, N+R5R6FW Z-; E = (mono/di/trialkyl)ammonioalkyl or a nucleic acid base conjugate; F = alkylene; R5, R6 = H, alkyl; W = OH, SH; Z- = anion]. Several compds. were prepared For example, etherification of isopropylideneglycerol with 1-bromododecane using KOH in PhMe and acid hydrolysis with HCl in MeOH-Et20 mixture gave 71% 3-dodecyloxy-1,2-propanediol. This underwent 1-O-tritylation with Ph3CCl in pyridine, 2-O-alkylation by 1-bromodecane and NaH in THF (51%), and detritylation by p-MeC6H4SO3H in CHC13-MeOH (63%) to give 3-dodecyloxy-2-decyloxy-1-propanol. The latter underwent esterification with (PhO) 2P(O)Cl (60%), hydrogenolysis of the Ph ester to the phosphatidic acid, and reesterification with AZT using DCC (22%) to give title compound (Na salt) I. Another compound, (±)-3-octadecanamido-2-ethoxypropyl-1-phosphocholine, inhibited HBV

т

virion DNA and intracellular RI HBV DNA in expts. to a comparable or

- greater extent than the standard agent ddC. 112989-01-2P 112989-02-3P RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 - study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of phospholipids for combating hepatitis B virus)
- RN 112989-01-2 CAPLUS CN 3.5-Dioxa-9-aza-4-phosphapentacosan-1-aminium.
 - 7-ethoxy-4-hydroxy-N, N, N-trimethyl-10-oxo-, inner salt, 4-oxide (CA INDEX NAME)

- RN 112989-02-3 CAPLUS
- CN 3.5-Dioxa-9-aza-4-phosphaheptacosan-1-aminium, 7-ethoxy-4-hydroxy-N, N, N-trimethyl-10-oxo-, inner salt, 4-oxide (CA INDEX NAME)

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD
(2 CITINGS)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1995:694404 CAPLUS

DOCUMENT NUMBER: 123:160151

ORIGINAL REFERENCE NO.: 123:28207a,28210a

TITLE: Membrane-interactive phospholipids inhibit HIV type

1-induced cell fusion and surface gp160/ gp120 binding

to monoclonal antibody
AUTHOR(S): Krugner-Higby, Lisa; Go

Krugner-Higby, Lisa; Goff, David; Edwards, Terri; Iver, Nathan; Neufeld, Jav; Kute, Timothy;

Morris-Natschke, Susan; Ishaq, Khalid; Piantadosi, Claude; Kucera, Louis S.

CORPORATE SOURCE: Wake Forest University, Winsto-Salem, NC, 27157-1064,

SOURCE: AIDS Research and Human Retroviruses (1995), 11(6),

705-12

CODEN: ARHRE7; ISSN: 0889-2229
PUBLISHER: Liebert

DOCUMENT TYPE: Journal LANGUAGE: English

English Membrane-interactive phospholipids (PLs), previously evaluated for AB activity against HIV-1 in vitro, are known to affect late steps in viral replication. Studies were done to determine the effects of PL analogs on post-translational processing of HIV-1 proteins, binding of viral surface qp160/qp120 to CD4 receptor, and HIV-1-induced cell fusion. Results of this investigation indicated that PL alone (1-octadecanamido-2-ethoxypropyl-rac-3-phosphocholine, CP-51) and PL-AZT conjugate (1-octadecanamido-2-ethoxypropyl-rac-3-phospho-3'-azido-3'deoxythymidine, CP-92) have no effect on HIV-1-induced syntheses or processing of gp160/gp120, pr51, p24, or p17 (including myristoylation) in infected cells. Progeny HIV-1 particles made in CP-92-treated H9IIIB cells contained qp120, pr51, and p24; however, these virus particles had reduced capacity to bind to CD4+ cells. Both CP-51 and CP-92 inhibited syncytium (cell fusion) formation between treated HIV-1-infected cells and uninfected CD4+ cells, and, they reduced HIV-1 gp160/gp120 binding to CD4+ cells and monoclonal antibody. These results suggest that anti-HIV-1 activity of PL compds. involves alteration of cell surface membranes and viral envelopes. Phospholipid compds. are a novel class of membrane interactive compds. with potential use in blocking the spread of HIV-1 infection and pathogenesis in AIDS.

II 112989-02-3, CP 51 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(membrane-interactive phospholipids inhibit HIV type 1-induced cell fusion and surface gp160/gp120 binding to monoclonal antibody)

RN 112989-02-3 CAPLUS

CN 3,5-Dioxa-9-aza-4-phosphaheptacosan-1-aminium,

7-ethoxy-4-hydroxy-N,N,N-trimethyl-10-oxo-, inner salt, 4-oxide (CA INDEX

OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)

L7 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 1991:185901 CAPLUS

DOCUMENT NUMBER: 114:185901

ORIGINAL REFERENCE NO.: 114:31415a,31418a

TITLE: Synthesis and evaluation of novel ether lipid nucleoside conjugates for anti-HIV-1 activity

AUTHOR(S): Piantadosi, Claude; Marasco, Canio J., Jr.;
Morris-Natschke, Susan L.; Meyer, Karen L.; Gumus,

Fatma; Surles, Jefferson R.; Ishaq, Khalid S.; Kucera,

Louis S.; Iyer, Nathan; et al.

CORPORATE SOURCE: Sch. Pharm., Univ. North Carolina, Chapel Hill, NC, 27599, USA

SOURCE: Journal of Medicinal Chemistry (1991), 34(4), 1408-14 CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 114:185901

GΙ

B Combinations of an amidoalkylphosphocholine,
C17H35CONNCH2CH(OE)(D102P(0)(0-)-OCH2CH2N+Me3, and AZT were found to cause
an apparent synergistic action in suppressing infectious HIV-1
replication. In addition, alkylamido, alkyloxy, and alkylthio ether lipids
were chemical linked to anti-HIV-1 nucleosides (AZT and DDI) through
phosphate and phosphonate linkages. These conjugates show promising in
vitro anti-HIV-1 activity. Also, the conjugates have a 5-10-fold reduction in
cell cytotoxicity compared to AZT alone. The most active compound, an
alkylamido ether lipid-AZT conjugate, I was found to have a differential
selectivity of 1793 in a syncytial plaque assay. In comparison, AZT alone

has a value of 1281.

112989-02-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(anti-HIV-1 activity of)

112989-02-3 CAPLUS

3,5-Dioxa-9-aza-4-phosphaheptacosan-1-aminium,

7-ethoxy-4-hydroxy-N, N, N-trimethyl-10-oxo-, inner salt, 4-oxide (CA INDEX NAME)

OS.CITING REF COUNT: 36 THERE ARE 36 CAPLUS RECORDS THAT CITE THIS RECORD (37 CITINGS)

L7 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2010 ACS on STN 1991:185881 CAPLUS

ACCESSION NUMBER: DOCUMENT NUMBER: 114:185881

ORIGINAL REFERENCE NO.: 114:31411a,31414a

TITLE: In vitro evaluation of phosphocholine and quaternary

ammonium containing lipids as novel anti-HIV agents AUTHOR(S): Meyer, Karen L.; Marasco, Canino J., Jr.;

Morris-Natschke, Susan L.; Ishaq, Khalid S.;

Piantadosi, Claude; Kucera, Louis S. CORPORATE SOURCE:

Sch. Pharm., Univ. North Carolina, Chapel Hill, NC,

27599, USA Journal of Medicinal Chemistry (1991), 34(4), 1377-83 SOURCE:

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal LANGUAGE: English

OTHER SOURCE(S): CASREACT 114:185881

GI

A series of synthetic lipids containing a two- or three-carbon backbone AB substituted with a thio, oxy, or amidoalkyl functionality and either a phosphocholine or quaternary ammonium moiety were evaluated as potential anti-HIV-1 agents. Several analogs were identified as possessing activity with the most promising compound being rac-3-octadecanamido-2-ethoxypropylphosphocholine (I). I exhibited an IC50 for the inhibition of plaque formation of 0.16 µM which was 84-fold lower than the IC50 value determined for CEM-SS cell growth inhibition. Initial mechanistic studies have indicated that these compds., unlike AZT, are not reverse transcriptase (RT) inhibitors, but instead appear to inhibit a late step in HIV replication involving virus assembly and infectious virus production. Since these lipids are acting via a different, mechanism they represent an alternative approach to the

chemotherapeutic treatment of AIDS as well as candidates for combination therapy with AZT.

- T 88876-07-7 112989-00-1 112989-01-2
 - 112989-02-3

RL: RCT (Reactant); RACT (Reactant or reagent)
 (anti-HIV-1 activity of)

- RN 88876-07-7 CAPLUS
- CN 3,5-Dioxa-9-aza-4-phosphaheptacosan-1-aminium, 4-hydroxy-7-methoxy-N,N,N-trimethyl-10-oxo-, inner salt, 4-oxide (CA INDEX NAME)

- RN 112989-00-1 CAPLUS
- CN 3,5-Dioxa-9-aza-4-phosphapentacosan-1-aminium, 4-hydroxy-7-methoxy-N,N,N-trimethyl-10-oxo-, inner salt, 4-oxide (9CI) (CA INDEX NAME)

- RN 112989-01-2 CAPLUS
- CN 3,5-Dioxa-9-aza-4-phosphapentacosan-1-aminium, 7-ethoxy-4-hydroxy-N,N,N-trimethyl-10-oxo-, inner salt, 4-oxide (CA INDEX NAME)

- RN 112989-02-3 CAPLUS
- CN 3,5-Dioxa-9-aza-4-phosphaheptacosan-1-aminium, 7-ethoxy-4-hydroxy-N,N,N-trimethyl-10-oxo-, inner salt, 4-oxide (CA INDEX NAME)

- IT 149576-20-5P
 - RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and anti-HIV-1 activity of)

149576-20-5 CAPLUS RN

CN 3,5-Dioxa-9-aza-4-phosphanonacosan-1-aminium,

7-ethoxy-4-hydroxy-N, N, N-trimethyl-10-oxo-, inner salt, 4-oxide (9CI) (CA INDEX NAME)

OEt. Me3+N-CH2-CH2-O-P-O-CH2-CH-CH2-NH-C-(CH2)18-Me

OS.CITING REF COUNT: 1.5 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)

L7 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2010 ACS on STN 1990:470710 CAPLUS

ACCESSION NUMBER: DOCUMENT NUMBER:

113:70710

ORIGINAL REFERENCE NO.: 113:11741a,11744a TITLE:

Novel membrane-interactive ether lipid analogs that inhibit infectious HIV-1 production and induce

defective virus formation

Kucera, Louis S.; Iyer, Nathan; Leake, Eva; Raben, AUTHOR(S):

Adam; Modest, Edward J.; Daniel, Larry W.; Piantadosi,

Claude

CORPORATE SOURCE: Bowman Grav Sch. Med., Wake Forest Univ.,

Winston-Salem, NC, 27103, USA

SOURCE . AIDS Research and Human Retroviruses (1990), 6(4), 491-501

CODEN: ARHRE7; ISSN: 0889-2229

DOCUMENT TYPE: Journal LANGUAGE: English

A new class of membrane-active ether lipid (EL) analogs of

platelet-activating factor were studied for in vitro anti-HIV-1 activity. Human T-cell (CEM-ss) monolayers or suspension cultures were used to determine effects of structural modifications of Type A phosphorus-containing and Type B nonphosphorus EL analogs on (a) the inhibitory concn.50 (IC50) for HIV-1 syncytial plaque formation and cell growth, and, (b) virus budding at the cell plasma membrane. Results indicate that representative Type A and Type B EL inhibit HIV-1 but not herpes simplex virus type 2 plaque formation when added before or up to 2 days after viral infection. Anti-HIV-1 activity does not involve direct inactivation of virus infectivity. Type A EL (IC50 range = 0.2-1.4 $\mu M)$ with alkoxy, alkylthio, or alkyamido substitution at glycerol position 1 and ethoxy or methoxy substitution at position 2, and Type B compds. (IC50 range = 0.33-0.63 μM) with an inverse choline or nitrogen heterocyclic substitution at position 3 have selective activity against HIV-1-infected T-cells. EL treatment of HIV-1-infected cells is associated with subsequent release of reverse transcriptase activity, but infectious virus production is inhibited with time after infection. Electron microscopic examination of HIV-1-infected and EL-treated cells revealed absence of detectable budding virus at the plasma membrane but presence of intracytoplasmic vacuolar virus

particles. EL analogs are a novel class of agents that induce defective intracytoplasmic vacuolar HIV-1 formation in T-cells. Being membrane

interactive, EL are ideally suited for combination chemotherapy with DNA-interactive anti-HIV nucleoside analogs.

112989-02-3

RL: BIOL (Biological study)

(human immunodeficiency virus infection response to)

RN 112989-02-3 CAPLUS

CN 3,5-Dioxa-9-aza-4-phosphaheptacosan-1-aminium, 7-ethoxy-4-hydroxy-N,N,N-trimethy1-10-oxo-, inner salt, 4-oxide (CA INDEX NAME)

OS.CITING REF COUNT: 31 THERE ARE 31 CAPLUS RECORDS THAT CITE THIS RECORD (32 CITINGS)

=> d his

(FILE 'HOME' ENTERED AT 12:41:35 ON 16 MAR 2010)

FILE 'REGISTRY' ENTERED AT 12:42:15 ON 16 MAR 2010 L1 STRUCTURE UPLOADED

L2 4 S L1 SSS

L3 47 S L1 FULL

FILE 'CAPLUS' ENTERED AT 12:43:06 ON 16 MAR 2010

L4 23 S L3 L5 23 DUP REM L4 (0 DUPLICATES REMOVED)

L6 23 S L5

L7 10 S L5 AND (VIRUS OR VIRAL)

=>

---Logging off of STN---

=>

Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS SINCE FILE TOTAL. ENTRY SESSION FULL ESTIMATED COST 64.72 264.88 DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL SESSION ENTRY CA SUBSCRIBER PRICE -8.50 -8.50

STN INTERNATIONAL LOGOFF AT 12:45:30 ON 16 MAR 2010